

CLAIMS

What is claimed is:

1. A method for preventing and/or treating an amyloid-related disease in a subject, comprising administering to a subject an antigenic amount of an all-D peptide which elicits production of antibodies against said all-D peptide, and elicit an immune response by said subject, therefore preventing fibrillogenesis and associated cellular toxicity, wherein said antibodies and/or immune cells interact with at least one region of an amyloid protein selected from the group consisting of β sheet region and GAG-binding site region, immunogenic fragments thereof, protein conjugates thereof, immunogenic derivative peptides thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof,.
2. The method of claim 1, wherein said compound is a compound of Formula I:

$$R'-(P)-R'' \text{ (I)}$$

wherein

P is an all-D peptide interacting with at least one region of an amyloid protein selected from the group consisting of β sheet region and GAG-binding site region, A β (1-42, all-D), immunogenic fragments thereof, immunogenic derivatives thereof, protein conjugates thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof;

R' is an N-terminal substituent selected from the group consisting of:

 - hydrogen;
 - lower alkyl groups selected from the group consisting of acyclic or cyclic having 1 to 8 carbon atoms;
 - aromatic groups;
 - heterocyclic groups; and
 - acyl groups; and

R'' is a C-terminal substituent selected from the group consisting of hydroxy, alkoxy, aryloxy, unsubstituted or substituted amino groups.
3. The method of claim 2, wherein said alkyl or aryl group of R' and R'' is further substituted with halide; hydroxyl, alkoxyl, aryloxy, hydroxycarbonyl, alkoxycarbonyl, aryloxy carbonyl, carbamyl, unsubstituted or substituted amino, sulfo or alkyloxysulfonyl, phosphono or alkoxyphosphonyl groups.

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4. The method of claim 2, wherein said compound further comprises an acid functional group, a pharmaceutically acceptable salt or ester form thereof; or a base functional group or pharmaceutically acceptable salt form thereof.
5. The method of claim 2, wherein said compound is selected from the group consisting of compounds 1 to 48.
6. The method of claim 5, wherein said compound is modified by removing or inserting one or more amino acid residues, or by substituting one or more amino acid residues with other amino acid or non-amino acid fragment.
7. The method of claim 6, wherein said compound is selected from the group consisting of compounds 49 to 63.
8. The method of claim 1, wherein said subject is a human being.
9. The method of claim 1, wherein said disease is Alzheimer's disease.
10. A vaccine for preventing and/or treating an amyloid-related disease in a subject, comprising an antibody raised against an antigenic amount of an all-D peptide which interacts with at least one region of an amyloid protein selected from the group consisting of β sheet region and GAG-binding site region, A β (1-42, all-D), immunogenic fragments thereof, protein conjugates thereof, immunogenic derivative peptides thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof, wherein said antibody interacts with amyloid proteins and therefore prevents fibrillogenesis.
11. The vaccine of claim 10, wherein said compound is a compound of Formula I:
$$R'-(P)-R'' \text{ (I)}$$

wherein

P is an all-D peptide interacting with at least one region of an amyloid protein selected from the group consisting of β sheet region and GAG-binding site region, A β (1-42, all-D), immunogenic fragments thereof, immunogenic derivatives thereof, protein conjugates thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof;

R' is an N-terminal substituent selected from the group consisting of:

hydrogen;
lower alkyl groups selected from the group consisting of acyclic or cyclic having
1 to 8 carbon atoms;
aromatic groups;
heterocyclic groups; and
acyl groups; and

R'' is a C-terminal substituent selected from the group consisting of hydroxy,
alkoxy, aryloxy, unsubstituted or substituted amino groups.

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12. The vaccine of claim 10, wherein said alkyl or aryl group of R' and R'' are further substituted with halide; hydroxyl, alkoxyl, aryloxy, hydroxycarbonyl, alkoxycarbonyl, aryloxy carbonyl, carbamyl, unsubstituted or substituted amino, sulfo or alkyloxysulfonyl, phosphono or alkoxyphosphonyl groups.
13. The vaccine of claim 11, wherein said compound further comprises an acid functional group, a pharmaceutically acceptable salt or ester form thereof; or a base functional group or pharmaceutically acceptable salt form thereof.
14. The vaccine of claim 10, wherein said compound is selected from the group consisting of compounds 1 to 48.
15. The vaccine of claim 11, wherein said compound is modified by removing or inserting one or more amino acid residues, or by substituting one or more amino acid residues with other amino acid or non-amino acid fragment.
16. The method of claim 15, wherein said compound is selected from the group consisting of compounds 49 to 63.
17. The vaccine of claim 10, wherein said subject is a human being.
18. The vaccine of claim 10, wherein said disease is Alzheimer's disease.
19. A method for preventing and/or treating an amyloid-related disease in a subject, comprising administering to said subject an antigenic amount of an all-D peptide which interacts with at least one region of an amyloid protein selected from the

group consisting of β sheet region and GAG-binding site region, immunogenic fragments thereof, protein conjugates thereof, immunogenic derivative peptides thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof, wherein said compound elicits an immune response by said subject and therefore prevents fibrillogenesis.

20. The method of claim 19, wherein said compound is a compound of Formula I:



wherein

P is an all-D peptide interacting with at least one region of an amyloid protein selected from the group consisting of β sheet region and GAG-binding site region, A β (1-42, all-D), immunogenic fragments thereof, immunogenic derivatives thereof, protein conjugates thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof;

R' is an N-terminal substituent selected from the group consisting of:
hydrogen;
lower alkyl groups selected from the group consisting of acyclic or cyclic having 1 to 8 carbon atoms;
aromatic groups;
heterocyclic groups; and
acyl groups; and

R'' is a C-terminal substituent selected from the group consisting of hydroxy, alkoxy, aryloxy, unsubstituted or substituted amino groups.

21. The method of claim 20, wherein said alkyl or aryl group of R' and R'' are further substituted with halide; hydroxyl, alkoxyl, aryloxy, hydroxycarbonyl, alkoxycarbonyl, aryloxy carbonyl, carbamyl, unsubstituted or substituted amino, sulfo or alkyloxysulfonyl, phosphono or alkoxyphosphonyl groups.

22. The method of claim 20, wherein said compound further comprises an acid functional group, a pharmaceutically acceptable salt or ester form thereof; or a base functional group or a pharmaceutically acceptable salt form thereof.

23. The method of claim 20, wherein said compound is selected from the group consisting of compounds 1 to 48.

24. The method of claim 23, wherein said compound is modified by removing or inserting one or more amino acid residues, or by substituting one or more amino acid residues with other amino acid or non-amino acid fragment.

25. The method of claim 24, wherein said compound is selected from the group consisting of compounds 49 to 63.

26. The method of claim 19, wherein said subject is a human being.

27. The method of claim 19, wherein said disease is Alzheimer's disease.

28. A method for preventing and/or treating of an amyloid related disease in a subject, which comprises administering to said subject an antigenic amount of a compound of Formula I:



wherein

P is an all-D peptide interacting with at least one region of an amyloid protein selected from the group consisting of β sheet region and GAG-binding site region, A β (1-42, all-D), immunogenic fragments thereof, immunogenic derivatives thereof, protein conjugates thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof;

R' is an N-terminal substituent selected from the group consisting of:
hydrogen;
lower alkyl groups selected from the group consisting of acyclic or cyclic having 1 to 8 carbon atoms;
aromatic groups;
heterocyclic groups; and
acyl groups; and

R'' is a C-terminal substituent selected from the group consisting of hydroxy, alkoxy, aryloxy, unsubstituted or substituted amino groups.

29. The method of claim 28, wherein said compound elicits an immune response by said subject and therefore prevents fibrillogenesis.

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30. The method of claim 28, wherein the alkyl or aryl group of R' and R'' are further substituted with halide; hydroxyl, alkoxyl, aryloxy, hydroxycarbonyl, alkoxycarbonyl, aryloxy carbonyl, carbamyl, unsubstituted or substituted amino, sulfo or alkyloxysulfonyl, phosphono or alkoxyphosphonyl groups.
- 5 31. The method of claim 30, wherein said compound has an acid functional group, a pharmaceutically acceptable salt or ester form thereof; or a base functional group or pharmaceutically acceptable salt thereof.
- 10 32. The method of claim 28, wherein said compound is selected from the group consisting of compounds 1 to 48.
- 15 33. The method of claim 32, wherein said compound is modified by removing or inserting one or more amino acid residues, or by substituting one or more amino acid residues with other amino acid or non-amino acid fragment.
34. The method of claim 33, wherein said compound is selected from the group consisting of compounds 49 to 63.
- 20 35. The method of claim 28, wherein said subject is a human being.
36. The method of claim 28, wherein said disease is Alzheimer's disease.
- 25 37. A vaccine for preventing and/or treating an amyloid-related disease in a subject, comprising an antigenic amount of an all-D peptide interacting with at least one region of an amyloid protein selected from the group consisting of β sheet region and GAG-binding site region, A β (1-42, all-D), immunogenic fragments thereof, protein conjugates thereof, immunogenic derivative peptides thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof, wherein said
- 30 compound elicits an immune response by said subject and therefore prevents fibrillogenesis.
38. The vaccine of claim 37, wherein said compound is a compound of Formula I:
- $$R'-(P)-R'' \quad (I),$$
- 35 wherein

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- 5 P is an all-D peptide interacting with at least one region of an amyloid protein selected from the group consisting of β sheet region and GAG-binding site region, A β (1-42, all-D), immunogenic fragments thereof, immunogenic derivatives thereof, protein conjugates thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof;
- R' is an N-terminal substituent selected from the group consisting of:
 hydrogen;
 lower alkyl groups selected from the group consisting of acyclic or cyclic having 1 to 8 carbon atoms;
 aromatic groups;
 heterocyclic groups; and
 acyl groups; and
- R'' is a C-terminal substituent selected from the group consisting of hydroxy, alkoxy, aryloxy, unsubstituted or substituted amino groups.
- 15 39. The vaccine of claim 38, wherein said alkyl or aryl group of R' and R'' is further substituted with halide; hydroxyl, alkoxyl, aryloxy, hydroxycarbonyl, alkoxycarbonyl, aryloxy carbonyl, carbamyl, unsubstituted or substituted amino, sulfo or alkyloxysulfonyl, phosphono or alkoxyphosphonyl groups.
- 20 40. The vaccine of claim 38, wherein said compound has an acid functional group, a pharmaceutically acceptable salt or ester form thereof; or said compound has a base functional group or pharmaceutically acceptable salt form thereof.
- 25 41. The vaccine of claim 37, wherein said compound is selected from the group consisting of compounds 1 to 48.
42. The vaccine of claim 38, wherein said compound is modified by removing or inserting one or more amino acid residues, or by substituting one or more amino acid residues with other amino acid or non-amino acid fragment.
- 30 43. The method of claim 42, wherein said compound is selected from the group consisting of compounds 49 to 63.
- 35 44. The vaccine of claim 37, wherein said subject is a human being.

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45. The vaccine of claim 37, wherein said disease is Alzheimer's disease.

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